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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	Feb 24	PCTGEN now available on STN
NEWS 4	Feb 24	TEMA now available on STN
NEWS 5	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 6	Feb 26	PCTFULL now contains images
NEWS 7	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 8	Mar 24	PATDPAFULL now available on STN
NEWS 9	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 10	Apr 11	Display formats in DGENE enhanced
NEWS 11	Apr 14	MEDLINE Reload
NEWS 12	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 13	AUG 22	Indexing from 1927 to 1936 added to records in CA/CAPLUS
NEWS 14	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 15	Apr 28	RDISCLOSURE now available on STN
NEWS 16	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS 17	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 18	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 19	May 19	Simultaneous left and right truncation added to WSCA
NEWS 20	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS 21	Jun 06	Simultaneous left and right truncation added to CBNB
NEWS 22	Jun 06	PASCAL enhanced with additional data
NEWS 23	Jun 20	2003 edition of the FSTA Thesaurus is now available
NEWS 24	Jun 25	HSDB has been reloaded
NEWS 25	Jul 16	Data from 1960-1976 added to RDISCLOSURE
NEWS 26	Jul 21	Identification of STN records implemented
NEWS 27	Jul 21	Polymer class term count added to REGISTRY
NEWS 28	Jul 22	INPADOC: Basic index (/BI) enhanced; Simultaneous Left and Right Truncation available
NEWS 29	AUG 05	New pricing for EUROPATFULL and PCTFULL effective August 1, 2003
NEWS 30	AUG 13	Field Availability (/FA) field enhanced in BEILSTEIN
NEWS 31	AUG 15	PATDPAFULL: one FREE connect hour, per account, in September 2003
NEWS 32	AUG 15	PCTGEN: one FREE connect hour, per account, in September 2003
NEWS 33	AUG 15	RDISCLOSURE: one FREE connect hour, per account, in September 2003
NEWS 34	AUG 15	TEMA: one FREE connect hour, per account, in September 2003
NEWS 35	AUG 18	Data available for download as a PDF in RDISCLOSURE
NEWS 36	AUG 18	Simultaneous left and right truncation added to PASCAL
NEWS 37	AUG 18	FROSTI and KOSMET enhanced with Simultaneous Left and Right Truncation

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 NEWS 38  AUG 18  Simultaneous left and right truncation added to ANABSTR

 NEWS EXPRESS  April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 13:44:44 ON 26 AUG 2003

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'REGISTRY' ENTERED AT 13:44:59 ON 26 AUG 2003
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STRUCTURE FILE UPDATES:   25 AUG 2003  HIGHEST RN 573649-48-6
DICTIONARY FILE UPDATES:  25 AUG 2003  HIGHEST RN 573649-48-6

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> s metformin hydrochloride
             9 METFORMIN
        593672 HYDROCHLORIDE
           138 HYDROCHLORIDES
        593672 HYDROCHLORIDE
                  (HYDROCHLORIDE OR HYDROCHLORIDES)
L1           2 METFORMIN HYDROCHLORIDE
                  (METFORMIN(W)HYDROCHLORIDE)

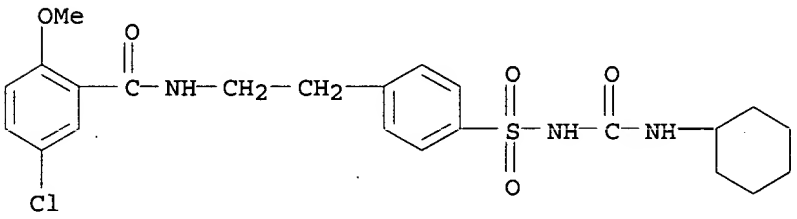
=> d L1 1-2

L1   ANSWER 1 OF 2  REGISTRY  COPYRIGHT 2003 ACS on STN
```

RN 338752-31-1 REGISTRY
CN Benzamide, 5-chloro-N-[2-[4-[[[(cyclohexylamino)carbonyl]amino]sulfonyl]phenyl]ethyl]-2-methoxy-, mixt. with N,N-dimethylimidodicarbonimidic diamide monohydrochloride (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Imidodicarbonimidic diamide, N,N-dimethyl-, monohydrochloride, mixt. contg. (9CI)
OTHER NAMES:
CN Glucovance
CN **Glyburide-metformin hydrochloride mixt.**
MF C23 H28 Cl N3 O5 S . C4 H11 N5 . Cl H
CI MXS
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

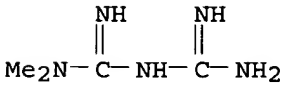
CM 1

CRN 10238-21-8
CMF C23 H28 Cl N3 O5 S



CM 2

CRN 1115-70-4 (657-24-9)
CMF C4 H11 N5 . Cl H

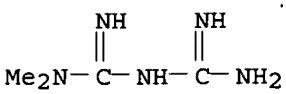


● HCl

7 REFERENCES IN FILE CA (1937 TO DATE)
7 REFERENCES IN FILE CAPLUS (1937 TO DATE)

L1 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2003 ACS on STN
RN 1115-70-4 REGISTRY
CN Imidodicarbonimidic diamide, N,N-dimethyl-, monohydrochloride (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Biguanide, 1,1-dimethyl-, hydrochloride (6CI)
CN Biguanide, 1,1-dimethyl-, monohydrochloride (8CI)
OTHER NAMES:
CN 1,1-Dimethylbiguanide hydrochloride
CN Apophage
CN Benofomin
CN Dabex
CN Denkaform
CN Dextin

CN Diabefagos
CN Diabetmin
CN Diabetosan
CN Diabex
CN Diaformin
CN Dialon
CN Diformin
CN Diformin Retard
CN Dimefor
CN Fornidd
CN Geamet
CN Glucaminol
CN Glucofago
CN Glucoform
CN Glucomet
CN Glucomin
CN Glucomine
CN Gluconil
CN Glucophage
CN Glucophage 850
CN Glucophage Forte
CN Glucophage Retard
CN Glucophage-Mite
CN Gludepatic
CN Glufor
CN Gluformin
CN Glumeformin
CN Glumin
CN Glupermin
CN Glyceriphage
CN Glyciphage
CN Glycon
CN Glyformin
CN LA 6023
CN Meguan
CN Metforal
CN **Metformin hydrochloride**
CN Metomin
CN Miformin
CN N,N-Dimethylbiguanide hydrochloride
CN N1,N1-Dimethylbiguanide hydrochloride
CN Orabet
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
DR 56258-19-6, 15537-72-1, 144377-16-2
MF C4 H11 N5 . Cl H
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DIOGENES, DRUGUPDATES, EMBASE, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MRCK*, MSDS-OHS, PHAR, PHARMASEARCH, PROMT, RTECS*, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)
CRN (657-24-9)



● HCl

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

250 REFERENCES IN FILE CA (1937 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
253 REFERENCES IN FILE CAPLUS (1937 TO DATE)
9 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	13.40	13.61

FILE 'CAPLUS' ENTERED AT 13:47:06 ON 26 AUG 2003
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FILE COVERS 1907 - 26 Aug 2003 VOL 139 ISS 9
FILE LAST UPDATED: 25 Aug 2003 (20030825/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s L1 and monolithic

259	L1
16588	MONOLITHIC
41	MONOLITHICS
16609	MONOLITHIC (MONOLITHIC OR MONOLITHICS)
L2 1	L1 AND MONOLITHIC

=> d L2 ibib abs hitrn

L2 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:940632 CAPLUS
DOCUMENT NUMBER: 137:389235
TITLE: Sustained release pharmaceutical compositions containing metformin and their preparation
INVENTOR(S): Gidwani, Suresh Kumar; Singnurkar, Purushottam; Tewari, Prashant Kumar
PATENT ASSIGNEE(S): USV Limited, India

SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002028181	A1	20020411	WO 2000-IB1404	20001002
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000073085	A5	20020415	AU 2000-73085	20001002
EP 1322158	A1	20030702	EP 2000-960937	20001002
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.: WO 2000-IB1404 A 20001002

AB **Monolithic** sustained-release pharmaceutical compn. comprises metformin hydrochloride as an active substance and a hydrophobic polymer and/or other hydrophobic material. The process of prepn. of the sustained release compn. includes granulating metformin hydrochloride and hydrophobic polymer and/or other hydrophobic material by hot melt granulation or by extrusion, and drying the granulated product. The dryed granulated product is compressed into tablets. The pharmaceutical compn. is used as an oral antihyperglycemic agent in the management of the non-insulin-dependent diabetes mellitus.

IT **1115-70-4**, Metformin hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sustained release pharmaceutical compns. contg.)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> s L1
L3          259 L1

=> s L1 and fatty acids
            259 L1
         323108 FATTY
             14 FATTIES
         323112 FATTY
                (FATTY OR FATTIES)
        1399869 ACIDS
         232789 FATTY ACIDS
                (FATTY(W)ACIDS)
L4           16 L1 AND FATTY ACIDS

=> s L3 and stearic
          60932 STEARIC
L5            9 L3 AND STEARIC

=> s L4 and binder and glidant and lubricant
         154042 BINDER
          73980 BINDERS
         179999 BINDER
                (BINDER OR BINDERS)
            122 GLIDANT
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            82 GLIDANTS
           165 GLIDANT
                 (GLIDANT OR GLIDANTS)
         59657 LUBRICANT
         65631 LUBRICANTS
         90091 LUBRICANT
                 (LUBRICANT OR LUBRICANTS)
L6           0 L4 AND BINDER AND GLIDANT AND LUBRICANT

=> s L1 and hot melt granulation
           259 L1
        374533 HOT
            34 HOTS
        374565 HOT
                 (HOT OR HOTS)
        268144 MELT
         77665 MELTS
        304589 MELT
                 (MELT OR MELTS)
         20118 GRANULATION
           844 GRANULATIONS
         20602 GRANULATION
                 (GRANULATION OR GRANULATIONS)
            14 HOT MELT GRANULATION
                 (HOT(W)MELT(W)GRANULATION)
L7           1 L1 AND HOT MELT GRANULATION

=> d L7 ibib abs hitrn

L7   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2002:940632  CAPLUS
DOCUMENT NUMBER:          137:389235
TITLE:                    Sustained release pharmaceutical compositions
                          containing metformin and their preparation
INVENTOR(S):              Gidwani, Suresh Kumar; Singnurkar, Purushottam;
                          Tewari, Prashant Kumar
PATENT ASSIGNEE(S):       USV Limited, India
SOURCE:                   PCT Int. Appl., 17 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.   DATE
     ---------------   ----  --------       ---------------   --------
     WO 2002028181      A1   20020411       WO 2000-IB1404    20001002
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
             YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
             CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 2000073085      A5   20020415       AU 2000-73085     20001002
     EP 1322158         A1   20030702       EP 2000-960937    20001002
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL
PRIORITY APPLN. INFO.:                    WO 2000-IB1404   A  20001002
AB   Monolithic sustained-release pharmaceutical compn. comprises metformin
     hydrochloride as an active substance and a hydrophobic polymer and/or
     other hydrophobic material.  The process of prepn. of the sustained
```

release compn. includes granulating metformin hydrochloride and hydrophobic polymer and/or other hydrophobic material by **hot melt granulation** or by extrusion, and drying the granulated product. The dryed granulated product is compressed into tablets. The pharmaceutical compn. is used as an oral antihyperglycemic agent in the management of the non-insulin-dependent diabetes mellitus.

IT **1115-70-4**, Metformin hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sustained release pharmaceutical compns. contg.)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d L4 1-16 ibib abs hitrn

L4 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:511116 CAPLUS
DOCUMENT NUMBER: 139:90449
TITLE: Formulations for controlled drug delivery to gastrointestinal tract
INVENTOR(S): Dong, Liang C.; Wong, Patrick S. L.; Espinal, Steve D.; Nguyen, Vu A.
PATENT ASSIGNEE(S): Alza Corporation, USA
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003053400	A1	20030703	WO 2002-US40763	20021219

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-343001P P 20011219

AB The present invention includes a formulation and controlled release dosage form that enable the controlled release of drugs showing reduced absorption in the lower gastrointestinal tract. The formulation of the present invention includes a drug that exhibits greater absorption in the upper GI tract than in the lower GI tract and a permeation enhancer, which serves to increase absorption of the drug in the lower GI tract. The formulation further includes a carrier that allows the formulation to transition to a bioadhesive gel in situ after the formulation is dispensed within the GI tract and has had some opportunity to reach the surface of the GI mucosal membrane. The bioadhesive gel formed by the formulation works to present effective concns. of both the drug and the permeation enhancer at the surface of the GI mucosal membrane over a period. The controlled release dosage form is designed to deliver the formulation of the present invention at a desired release rate or release rate profile over a desired period of time. Thus, a formulation contained L-Dopa 33.3, carbidopa 8.3, lauric acid 14, and Cremopho-EL 44.4%.

IT **1115-70-4**, Metformin hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(formulations for controlled drug delivery to upper gastrointestinal tract)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:48383 CAPLUS
DOCUMENT NUMBER: 138:130894
TITLE: Metformin versus ethinyl estradiol-cyproterone acetate in the treatment of nonobese women with polycystic ovary syndrome: A randomized study
AUTHOR(S): Morin-Papunen, Laure; Vauhkonen, Ilkka; Koivunen, Riitta; Ruokonen, Aimo; Martikainen, Hannu; Tapanainen, Juha S.
CORPORATE SOURCE: Departments of Obstetrics and Gynecology, University Hospital of Oulu, Oulu, FIN-90014, Finland
SOURCE: Journal of Clinical Endocrinology and Metabolism (2003), 88(1), 148-156
CODEN: JCEMAZ; ISSN: 0021-972X
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Metformin, an insulin-sensitizing drug, has been shown to improve ovarian function and glucose metab. in obese women with polycystic ovary syndrome (PCOS), but its effects and possible benefits in nonobese PCOS subjects are not well known. Seventeen nonobese (body mass index < 25 kg/m2) women with PCOS were randomized to receive either metformin (500 mg twice daily for 3 mo, then 1000 mg twice daily for 3 mo; n = 8) or ethinyl estradiol (EE, 35 .mu.g)-cyproterone acetate (CA, 2 mg) oral contraceptive pills (EE-CA; n = 9). Waist to hip ratio; serum concns. of sex steroids, glucose, and insulin during a 75-g oral glucose tolerance test; early phase insulin and C-peptide secretion; and insulin sensitivity using a euglycemic hyperinsulinemic clamp were assessed at baseline and at 3 and 6 mo of treatment. Metformin did not have any effect on glucose tolerance or insulin sensitivity, but fasting insulin concns. decreased from 44.4 .+-. 5.1 (SE) to 29.8 .+-. 4.3 pmol/L (P = 0.03), the waist to hip ratio decreased from 0.78 .+-. 0.01 to 0.75 .+-. 0.01 (P = 0.01), and hepatic insulin clearance increased during the treatment. Furthermore, metformin decreased serum testosterone levels from 2.7 .+-. 0.3 to 2.0 .+-. 0.2 nmol/L (P = 0.01) and improved menstrual cyclicity. EE-CA did not have any significant effect on glucose tolerance, serum insulin levels, or insulin sensitivity, but it increased slightly the body mass index (P = 0.09) and significantly serum leptin concns. (P < 0.001) and decreased serum testosterone levels from 2.1 .+-. 0.2 to 1.4 .+-. 0.2 nmol/L (P = 0.03). In conclusion, EE-CA seems to be an efficient mode of therapy for hyperandrogenic symptoms assocd. with PCOs, but its possible neg. effects on insulin and glucose metab. also have to be taken into consideration in nonobese subjects. Metformin improved hyperandrogenism, hyperinsulinemia, and menstrual cyclicity, most likely through its pos. effect on insulin clearance and abdominal adiposity. Thus, similarly to obese PCOS women, nonobese PCOS subjects with anovulation may also benefit from metformin treatment.
IT **1115-70-4**, Diformin
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metformin (Diformin) vs. ethinyl estradiol-cyproterone acetate in treatment of nonobese women with polycystic ovary syndrome (PCOS))
REFERENCE COUNT: 86 THERE ARE 86 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:42092 CAPLUS
DOCUMENT NUMBER: 138:112443
TITLE: Tablet compositions for poorly-compressible pharmaceuticals
INVENTOR(S): Matharu, Amol Singh; Patel, Mahendra R.

PATENT ASSIGNEE(S): Geneva Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003004009	A1	20030116	WO 2002-US20323	20020627
US 2003021841	A1	20030130	US 2002-183881	20020627

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-302613P P 20010702

AB The present invention relates to a process for prepg. tablet dosage forms of poorly-compressible pharmaceuticals and to tablet dosage forms. The process is esp. useful for prepg. tablets of the poorly-compressible drug metformin-HCl. Thus, tablets contained metformin-HCl 500, HPMC 320, stearyl alc. 200, and Mg stearate mg/unit.

IT **1115-70-4**, Metformin hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tablet compns. for poorly-compressible pharmaceuticals)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:966701 CAPLUS
DOCUMENT NUMBER: 138:33149
TITLE: Effect of combination glipizide GITS/metformin on fibrinolytic and metabolic parameters in poorly controlled type 2 diabetic subjects
AUTHOR(S): Cefalu, William T.; Schneider, David J.; Carlson, Harold E.; Migdal, Phyllis; Lim, Leonil Gan; Izon, Meriam P.; Kapoor, Anoop; Bell-Farrow, Audrey; Terry, James G.; Sobel, Burton E.
CORPORATE SOURCE: Department of Medicine, University of Vermont College of Medicine, Burlington, VT, USA
SOURCE: Diabetes Care (2002), 25(12), 2123-2128
CODEN: DICAD2; ISSN: 0149-5992
PUBLISHER: American Diabetes Association, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB OBJECTIVE: Epidemiol. studies have implicated increased plasminogen-activated inhibitor I (PAI-1) as a marker or predictor of accelerated coronary atherosclerotic disease in type 2 diabetes. We sought to det. whether metabolic control, independent of its oral mode of implementation, affects PAI-1 in patients with marked hyperglycemia. RESEARCH DESIGN AND METHODS: A total of 91 subjects were screened, subjected to a 4-wk drug washout, and randomized to daily treatment with glipizide GITS (max. 20 mg, n = 46) or metformin (max. 2,550 mg, n = 45) as monotherapy. After monotherapy, combination therapy was initiated by adding the second agent to the regimen. Plasma glucose (fasting and postprandial), HbA1c, fructosamine, and PAI-1 were assayed before and after randomization and sequentially thereafter in all subjects; hepatic glucose output (HGO) and abdominal fat distribution were each measured in

a subset of subjects. RESULTS: Glycemic control was markedly impaired at baseline (mean HbA1c 10.4.+-.0.2% glipizide GITS; 10.0.+-.0.2% metformin) but improved comparably with each agent as monotherapy and in combination ($P < 0.0001$ vs. baseline), as assessed with meal tolerance studies, fructosamine values, and HGO. Body wt. and abdominal fat distribution did not change significantly in either group. PAI-1 concns. were extraordinarily high (5- to 10-fold more than normal) at baseline (202.+-.12 ng/mL glipizide GITS; 201.+-.13 ng/mL metformin) but declined comparably, and significantly, after treatment with either agent as monotherapy and decreased further with combination therapy. CONCLUSIONS: When hyperglycemia is profound, increases in PAI-1 are also profound. Control of hyperglycemia with either glipizide GITS, an insulin secretagogue, or metformin as monotherapy comparably ameliorates elevated PAI-1.

IT **1115-70-4**, Glucophage
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glipizide GITS (Glucotrol XL) and metformin (Glucophage) monotherapy vs. combination therapy effects on fibrinolytic and metabolic parameters in type 2 diabetic mellitus patients)

L4 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:940632 CAPLUS
DOCUMENT NUMBER: 137:389235
TITLE: Sustained release pharmaceutical compositions containing metformin and their preparation
INVENTOR(S): Gidwani, Suresh Kumar; Singnurkar, Purushottam; Tewari, Prashant Kumar
PATENT ASSIGNEE(S): USV Limited, India
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002028181	A1	20020411	WO 2000-IB1404	20001002
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000073085	A5	20020415	AU 2000-73085	20001002
EP 1322158	A1	20030702	EP 2000-960937	20001002
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.: WO 2000-IB1404 A 20001002

AB Monolithic sustained-release pharmaceutical compn. comprises metformin hydrochloride as an active substance and a hydrophobic polymer and/or other hydrophobic material. The process of prepn. of the sustained release compn. includes granulating metformin hydrochloride and hydrophobic polymer and/or other hydrophobic material by hot melt granulation or by extrusion, and drying the granulated product. The dryed granulated product is compressed into tablets. The pharmaceutical compn. is used as an oral antihyperglycemic agent in the management of the non-insulin-dependent diabetes mellitus.

IT **1115-70-4**, Metformin hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(sustained release pharmaceutical compns. contg.)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:845479 CAPLUS
DOCUMENT NUMBER: 137:342124
TITLE: Biphasic controlled-release delivery systems for high solubility pharmaceuticals
INVENTOR(S): Timmins, Peter; Dennis, Andrew B.; Vyas, Kiren A.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: U.S., 16 pp., Cont.-in-part of U.S. Ser. No. 44,446, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6475521	B1	20021105	US 1999-398107	19990916

PRIORITY APPLN. INFO.: US 1998-44446 B2 19980319
AB A biphasic controlled release delivery system for pharmaceuticals which have high water soly., such as the antidiabetic, metformin-HCl, provides a dosage form that has prolonged gastric residence so that a dosing regimen of at least one gram metformin, once daily, may be achieved while providing effective control of plasma glucose. The delivery system includes (1) an inner solid particulate phase formed of substantially uniform granules contg. a pharmaceutical having a high water soly., and 1 or more hydrophilic polymers, 1 or more hydrophobic polymers and/or one or more hydrophobic materials such as 1 or more waxes, fatty alcs. and/or fatty acid esters, and (2) an outer solid continuous phase in which the above granules of inner solid particulate phase are embedded and dispersed throughout, the outer solid continuous phase including hydrophilic polymers, hydrophobic polymers and/or hydrophobic materials such as waxes, fatty alcs. and/or fatty acid esters, which may be compressed into tablets or filled into capsules. Methods for forming the so-described biphasic controlled release delivery system and using such biphasic controlled release delivery system for treating diabetes are also provided. Et cellulose N10 NF (25 g) was dissolved/dispersed in 100 mL ETOH. This dispersion was gradually added to 500 g metformin-HCl in a planetary mixer to produce a uniform damp granulation. The granulation was dried at 55.degree. for 1 h and passed through a 0.8-mm aperture screen to break down agglomerates. The metformin-Et cellulose granules (541 g) were blended with 351.5 g hydroxypropyl Me cellulose 2208 USP (100,000 cps grade), 10 g hydroxypropyl Me cellulose 2910 USP, and 100.5 g microcryst. cellulose in a planetary mixer for 10 min. Finally this mix was lubricated with 1% MG stearate and compressed into capsule-shaped tablets, each contg. 500 mg metformin-HCl.
IT **1115-70-4**, Metformin hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biphasic controlled-release delivery systems for high soly. pharmaceuticals)
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:391499 CAPLUS
DOCUMENT NUMBER: 136:406855
TITLE: Medicine based on antihyperglycemic microcapsules with prolonged release and method for preparing same
INVENTOR(S): Castan, Catherine; Meyrueix, Remi; Soula, Gerard
PATENT ASSIGNEE(S): Flamel Technologies, Fr.

SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002039984	A2	20020523	WO 2001-FR3625	20011119
WO 2002039984	A3	20020711		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
FR 2816840	A1	20020524	FR 2000-14876	20001117
AU 2002020796	A5	20020527	AU 2002-20796	20011119
EP 1333816	A2	20030813	EP 2001-996365	20011119
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: FR 2000-14876 A 20001117
WO 2001-FR3625 W 20011119

AB The invention concerns an oral galenic form for prolonged release of anti-hyperglycemic (metformin) active principles. Said medicine enables to obtain an efficient therapeutic protection over 24 h by overcoming the problems of bypass of the absorption window and the massive localized release of active principles. Therefor, said medicine comprises several thousand anti- hyperglycemic (metformin) microcapsules each consisting of a core comprising at least an anti- hyperglycemic agent and of a coating film applied on the core and enabling the prolonged release in vivo of the anti- hyperglycemic agent. Said microcapsules have a grain size distribution ranging between 50 and 100 .mu.. The reproducibility of the transit kinetics and hence of bioavailability are very high. There results for the patient a lesser risk of hyperglycemic or hypoglycemic. The invention also concerns the prepn. of said medicine and the use of a plurality of said microcapsules for making an anti- hyperglycemic medicine. The invention is applicable to the treatment of type II diabetes. A soln. of 159.5 g stearic acid and 159.5 g Et cellulose in 2870 g isopropanol at 50.degree. was sprayed on 700 g of metformin hydrochloride crystals (av. diam. 100-200 .mu.m). The dissoln. rate of the granules thus obtained was 97.1% after 20 min.

IT **1115-70-4**, Metformin hydrochloride
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medicine based on antihyperglycemic microcapsules with prolonged release and method for prepg. same)

L4 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:51243 CAPLUS
DOCUMENT NUMBER: 136:123633
TITLE: Oral pharmaceutical composition with controlled release and prolonged absorption
INVENTOR(S): Castan, Catherine; Legrand, Valerie; Meyrueix, Remi; Soula, Gerard
PATENT ASSIGNEE(S): Flamel Technologies, Fr.
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002003964	A1	20020117	WO 2001-FR2224	20010710
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2811571	A1	20020118	FR 2000-9047	20000711
FR 2811571	B1	20021011		
EP 1299090	A1	20030409	EP 2001-955397	20010710
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: FR 2000-9047 A 20000711
WO 2001-FR2224 W 20010710

AB The invention concerns a galenic system with prolonged/controlled release of the medicinal and/or nutritional active principle, for oral administration. The aim is to provide a system enabling to obtain with one single tolerable and acceptable dose of active principle, efficient therapeutic protection over 24 h (increasing the bioabsorption time without affecting bioavailability). To achieve this, the invention provides a compn. comprising two controlled release systems assocd. in series, namely: individualized coated particles (microcapsules) of active principle forming an internal phase, the coating comprising a film-forming polymer P1 (Et cellulose), a nitrogenous polymer (polyvinylpyrrolidone), a softener (castor oil) and a lubricant (magnesium stearate), and an external phase of functional carriers: polyelectrolytic hydrophilic polymer: (alginate), neutral hydrophilic polymer (hydroxypropyl Me cellulose) and a gelling additive (calcium acetate), said compn. spontaneously forming in the presence of water, a cohesive and stable composite macroscopic solid, wherein the external continuous phase is a gelled matrix including the active principle microcapsules. The invention is useful for delayed oral galenic formulation of metformin. A capsule contained metformine hydrochloride 25.47, Ethocel-7 6.60, magnesium stearate 0.89, castor oil 0.72, Plasdone K 29/32 0.72, Kelton HVCR 50.91, Methocel premium K100M 13.12, and calcium acetate 1.57%. Dissoln. rate of the capsule was studied.

IT **1115-70-4**, Metformin hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral pharmaceutical compn. with controlled release and prolonged absorption)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:396644 CAPLUS
DOCUMENT NUMBER: 135:24671
TITLE: Solid carriers for improved delivery of active ingredients in pharmaceutical compositions
INVENTOR(S): Patel, Manesh V.; Chen, Feng-jing
PATENT ASSIGNEE(S): Lipocine, Inc., USA
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001037808	A1	20010531	WO 2000-US32255	20001122
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6248363	B1	20010619	US 1999-447690	19991123
EP 1233756	A1	20020828	EP 2000-980761	20001122
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003517470	T2	20030527	JP 2001-539423	20001122

PRIORITY APPLN. INFO.: US 1999-447690 A 19991123
WO 2000-US32255 W 20001122

AB The present invention provides solid pharmaceutical compns. for improved delivery of a wide variety of pharmaceutical active ingredients contained therein or sep. administered. In one embodiment, the solid pharmaceutical compn. includes a solid carrier, the solid carrier including a substrate and an encapsulation coat on the substrate. The encapsulation coat can include different combinations of pharmaceutical active ingredients, hydrophilic surfactant, lipophilic surfactants and triglycerides. In another embodiment, the solid pharmaceutical compn. includes a solid carrier, the solid carrier being formed of different combinations of pharmaceutical active ingredients, hydrophilic surfactants, lipophilic surfactants and triglycerides. The compns. of the present invention can be used for improved delivery of hydrophilic or hydrophobic pharmaceutical active ingredients, such as drugs, nutritionals, cosmeceuticals and diagnostic agents. A compn. contained glyburide 1, PEG 40 stearate 33, glycerol monolaurate 17, and nonpareil seed 80 g. .

IT **1115-70-4**, Metformin hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(solid carriers for improved delivery of active ingredients in pharmaceutical compns.)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:300514 CAPLUS
DOCUMENT NUMBER: 134:331617
TITLE: Oil-in-water emulsion compositions for polyfunctional active ingredients
INVENTOR(S): Chen, Feng-jing; Patel, Mahesh V.
PATENT ASSIGNEE(S): Lipocine, Inc., USA
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001028555	A1	20010426	WO 2000-US28835	20001018
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002107265 A1 20020808 US 1999-420159 19991018

PRIORITY APPLN. INFO.: US 1999-420159 A 19991018

AB Pharmaceutical oil-in-water emulsions for delivery of polyfunctional active ingredients with improved loading capacity, enhanced stability, and reduced irritation and local toxicity are described. Emulsions include an aq. phase, an oil phase comprising a structured triglyceride, and an emulsifier. The structured triglyceride of the oil phase is substantially free of triglycerides having three medium chain (C6-C12) fatty acid moieties, or a combination of a long chain triglyceride and a polarity-enhancing polarity modifier. The present invention also provides methods of treating an animal with a polyfunctional active ingredient, using dosage forms of the pharmaceutical emulsions. For example, an emulsion was prepd., with cyclosporin A as the polyfunctional active ingredient dissolved in an oil phase including a structured triglyceride (Captex 810D) and a long chain triglyceride (safflower oil). The compn. contained (by wt.) cyclosporin A 1.0, Captex 810D 5.0, safflower oil 5.0, BHT 0.02, egg phospholipid 2.4, dimyristoylphosphatidyl glycerol 0.2, glycerol 2.25, EDTA 0.01, and water up to 100%, resp.

IT **1115-70-4**, Metformin hydrochloride

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(oil-in-water emulsion compns. for polyfunctional active ingredients)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:136991 CAPLUS

DOCUMENT NUMBER: 134:198075

TITLE: Triglyceride-free compositions and methods for enhanced absorption of hydrophilic therapeutic agents

INVENTOR(S): Patel, Mahesh V.; Chen, Feng-Jing

PATENT ASSIGNEE(S): Lipocine, Inc., USA

SOURCE: PCT Int. Appl., 113 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 8

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001012155	A1	20010222	WO 2000-US18807	20000710
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6309663	B1	20011030	US 1999-375636	19990817
EP 1210063	A1	20020605	EP 2000-947184	20000710
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003506476	T2	20030218	JP 2001-516502	20000710
US 2001024658	A1	20010927	US 2000-751968	20001229
US 6458383	B2	20021001		

PRIORITY APPLN. INFO.: US 1999-375636 A 19990817
WO 2000-US18807 W 20000710

AB The present invention relates to triglyceride-free pharmaceutical compns., pharmaceutical systems, and methods for enhanced absorption of hydrophilic

therapeutic agents. The compns. and systems include an absorption enhancing carrier, where the carrier is formed from a combination of at least two surfactants, at least one of which is hydrophilic. A hydrophilic therapeutic agent can be incorporated into the compn., or can be co-administered with the compn. as part of a pharmaceutical system. The invention also provides methods of treatment with hydrophilic therapeutic agents using these compns. and systems. For example, when a compn. contg. Cremophor RH40 0.30, Arlacel 186 0.20, Na taurocholate 0.18, and propylene glycol 0.32 g, resp., was used, the relative absorption of PEG 4000 as a model macromol. drug was enhanced by 991%.

IT **1115-70-4**, Metformin hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. for enhanced absorption of hydrophilic drugs using combination of surfactants)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:766143 CAPLUS
DOCUMENT NUMBER: 131:356089
TITLE: Oral immediate- or long-term release metformin-based galenic tablets comprising polyglycolyzated glycerides as an absorption promoters
INVENTOR(S): Saslawski, Olivier; Giet, Philippe; Michel, Dominique; Hulot, Thierry
PATENT ASSIGNEE(S): LIPHA, Lyonnaise Industrielle Pharmaceutique S. A., Fr.
SOURCE: Fr. Demande, 46 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2776189	A1	19990924	FR 1999-7284	19990609

PRIORITY APPLN. INFO.: FR 1999-7284 19990609

AB Oral immediate- or long-term release pharmaceutical tablets contain metformin and polyglycolyzated glycerides having HLB>8 as absorption promoters. An immediate-release pharmaceutical tablet contained calcium acamprosate 47, Gelucire 44/14 39, Labrasol 13, soya lecithin 1% (HLB = 14).

IT **1115-70-4**, Metformin hydrochloride
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(oral immediate- or long-term release metformin-based galenic tablets comprising polyglycolyzated glycerides as absorption promoters)

L4 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:613646 CAPLUS
DOCUMENT NUMBER: 131:233580
TITLE: Controlled release oral tablet having a unitary core
INVENTOR(S): Cheng, Xiu Xiu; Chen, Chih-Ming; Jan, Steve; Chou, Joseph
PATENT ASSIGNEE(S): Andrx Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9947125	A1	19990923	WO 1999-US6024	19990319	
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,				
	DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG,				
	KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,				
	NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,				
	UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,				
	ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,				
	CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6099859	A	20000808	US 1998-45330	19980320	
CA 2324493	AA	19990923	CA 1999-2324493	19990319	
AU 9931019	A1	19991011	AU 1999-31019	19990319	
AU 739226	B2	20011004			
EP 1063971	A1	20010103	EP 1999-912705	19990319	
R:	CH, DE, DK, ES, FR, GB, IT, LI, NL, SE				
JP 2002506810	T2	20020305	JP 2000-536365	19990319	
US 2001024659	A1	20010927	US 2000-726193	20001129	
US 2002064556	A1	20020530	US 2001-16556	20011101	
US 6495162	B2	20021217			

PRIORITY APPLN. INFO.:	US 1998-45330	A	19980320
	WO 1999-US6024	W	19990319
	US 2000-594637	A1	20000615

AB A controlled release antihyperglycemic tablet that does not contain an expanding polymer comprises a core contg. the antihyperglycemic drug, a semipermeable membrane coating the core and at least one passageway in the membrane. A core was prepd. contg. metformin-HCL 90.54, Povidone 4.38, Na3PO4 4.58, and Mg stearate 0.5% and a sustained release coting comprised cellulose acetate 85, triacetin 5, and PEG 400 10%.

IT **1115-70-4**, Metformin hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled release oral tablet having a unitary core)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER:	1999:549136 CAPLUS
DOCUMENT NUMBER:	131:161654
TITLE:	Orally administrable immediate-release and prolonged-release galenic form comprising an absorption-promoting agent
INVENTOR(S):	Saslawski, Olivier; Giet, Philippe; Michel, Dominique; Hulot, Thierry
PATENT ASSIGNEE(S):	Merck Patent G.m.b.H., Germany
SOURCE:	PCT Int. Appl., 65 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

WO 9942086	A1	19990826	WO 1999-EP994	19990216	
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,				
	DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,				
	KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,				
	MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,				
	TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU,				
	TJ, TM				
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,				
	FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,				
	CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2775188	A1	19990827	FR 1998-2143	19980223	

FR 2775188	B1	20010309			
CA 2321267	AA	19990826	CA 1999-2321267	19990216	
AU 9931408	A1	19990906	AU 1999-31408	19990216	
AU 750785	B2	20020725			
BR 9908121	A	20001024	BR 1999-8121	19990216	
EP 1056445	A1	20001206	EP 1999-913165	19990216	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO					
JP 2002503686	T2	20020205	JP 2000-532103	19990216	
ZA 9901408	A	19990823	ZA 1999-1408	19990222	
NO 2000004190	A	20001020	NO 2000-4190	20000822	
US 6426087	B1	20020730	US 2000-622663	20000822	
US 6514524	B1	20030204	US 2002-100084	20020319	

PRIORITY APPLN. INFO.: FR 1998-2143 A 19980223
WO 1999-EP994 W 19990216
US 2000-622633 A1 20000822

OTHER SOURCE(S): MARPAT 131:161654

AB The present invention relates to an orally administrable galenic form allowing improved absorption by the transmembrane or paracellular route in the gastrointestinal tract of active ingredients which are hydrophilic or ionizable in physiol. media, comprising at least one such active ingredient, an absorption-promoting agent having an HLB >8, the the absorption-promoting agent consisting of one or more lipid substances chosen from: polysorbates; polyoxyethylene ethers; esters of polyoxyethylene and **fatty acids**; **fatty acids**; fatty alcs.; bile acids and their salts with pharmaceutically acceptable cations; esters of C1-C6 alkanol with **fatty acids**; esters of polyol with **fatty acids**, the polyol comprising from 2 to 6 hydroxyl functional groups; and polyglycolyzed glycerides; in combination with one or more pharmaceutically acceptable excipients, the pharmaceutical forms comprising captopril being excluded. A controlled-release tablet contained (1) cores contg. calcium acamprosate 50, Gelucire 44/14 10, Compritol 10, microcryst. cellulose 19, Povidone 10, and Mg stearate 1 % and (2) a film-coating compn. contg. HPMC 64, PEG-4000 15, and talc 21 %.

IT **1115-70-4**, Metformin hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(absorption-promoting agents for controlled-release oral pharmaceuticals)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1979:20248 CAPLUS
DOCUMENT NUMBER: 90:20248
TITLE: Studies on certain serum components of treated and newly detected maturity onset diabetics and nondiabetics
AUTHOR(S): George, K. A.; Augusti, K. T.; Roy, V. C. M.
CORPORATE SOURCE: Dep. Biochem., Univ. Kerala, Trivandrum, India
SOURCE: Indian Journal of Experimental Biology (1978), 16(10), 1052-6
CODEN: IJEBA6; ISSN: 0019-5189
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Serum components of treated maturity onset diabetics were compared with those of newly detected diabetics and non-diabetics; relation of age, obesity and serum parameters with the control of blood sugar by various treatments were analyzed. Insulin, glibenclamide, chloropropamide and some biguanides were used by different groups. Even though insulin and hypoglycemics controlled the blood sugar, their effects on blood sugar, serum pyruvate, free **fatty acids**, total cholesterol, phospholipids, triglycerides and lipoproteins were not similar. Insulin alone lowered the pyruvate level; except insulin all the other drugs

caused a redn. in the free **fatty acids**. Only insulin and glibenclamide exerted a lowering effect on triglycerides. There was no indication of any relation of age and obesity with respect to triglycerides and control of blood sugar. Hyperlipoproteinemia (abnormal amts. of lipoproteins in blood) of type IV was found mainly in all the diabetic groups. However, treatment did not increase any of the parameters studied over the diabetics control.

IT **1115-70-4**
RL: BIOL (Biological study)
(blood serum compn. response to, in diabetes)

L4 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1975:80357 CAPLUS
DOCUMENT NUMBER: 82:80357
TITLE: Effects of biguanides on fatty acid and glucose oxidation in muscle
AUTHOR(S): Corsini, G. U.; Sirigu, F.; Tagliamonte, P.; Muntoni, S.
CORPORATE SOURCE: Dep. Pharmacol. Chemother., Univ. Cagliari, Cagliari, Italy
SOURCE: Pharmacological Research Communications (1974), 6(3), 253-61
CODEN: PLRCAT; ISSN: 0031-6989
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The biguanides, phenformin-HCl [834-28-6] and metformin-HCl [**1115-70-4**], inhibited glucose [50-99-7] metab. by rat diaphragm homogenate via depression of fatty acid oxidn. The biguanides decreased 14CO2 prodn. from 14C-labeled palmitic acid [57-10-3], but not from 14C-labeled glucose. The inhibition of 14C-labeled glucose oxidn. by unlabeled palmitic acid was partly removed by biguanides.

IT **1115-70-4**
RL: BIOL (Biological study)
(glucose metab. response to, fatty acid metab. in relation to)

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L5 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:435090 CAPLUS
DOCUMENT NUMBER: 138:406982
TITLE: Metformin hydrochloride tablets
INVENTOR(S): Sherman, Bernard Charles
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 4 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003104049	A1	20030605	US 2001-2130	20011205

PRIORITY APPLN. INFO.: US 2001-2130 20011205

AB Tablets for oral administration comprising metformin hydrochloride and methylcellulose are disclosed.

IT **1115-70-4**, Metformin hydrochloride
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(metformin hydrochloride tablets)

L5 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2003:42092 CAPLUS
DOCUMENT NUMBER: 138:112443
TITLE: Tablet compositions for poorly-compressible pharmaceuticals
INVENTOR(S): Matharu, Amol Singh; Patel, Mahendra R.
PATENT ASSIGNEE(S): Geneva Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003004009	A1	20030116	WO 2002-US20323	20020627

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003021841	A1	20030130	US 2002-183881	20020627

PRIORITY APPLN. INFO.: US 2001-302613P P 20010702

AB The present invention relates to a process for prepg. tablet dosage forms of poorly-compressible pharmaceuticals and to tablet dosage forms. The process is esp. useful for prepg. tablets of the poorly-compressible drug metformin-HCl. Thus, tablets contained metformin-HCl 500, HPMC 320, stearyl alc. 200, and Mg stearate mg/unit.

IT **1115-70-4**, Metformin hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tablet compns. for poorly-compressible pharmaceuticals)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:940632 CAPLUS
DOCUMENT NUMBER: 137:389235
TITLE: Sustained release pharmaceutical compositions containing metformin and their preparation
INVENTOR(S): Gidwani, Suresh Kumar; Singnurkar, Purushottam; Tewari, Prashant Kumar
PATENT ASSIGNEE(S): USV Limited, India
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002028181	A1	20020411	WO 2000-IB1404	20001002

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2000073085	A5	20020415	AU 2000-73085	20001002
EP 1322158	A1	20030702	EP 2000-960937	20001002

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL

PRIORITY APPLN. INFO.: WO 2000-IB1404 A 20001002

AB Monolithic sustained-release pharmaceutical compn. comprises metformin hydrochloride as an active substance and a hydrophobic polymer and/or other hydrophobic material. The process of prepn. of the sustained release compn. includes granulating metformin hydrochloride and hydrophobic polymer and/or other hydrophobic material by hot melt granulation or by extrusion, and drying the granulated product. The dryed granulated product is compressed into tablets. The pharmaceutical compn. is used as an oral antihyperglycemic agent in the management of the non-insulin-dependent diabetes mellitus.

IT **1115-70-4**, Metformin hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sustained release pharmaceutical compns. contg.)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:391499 CAPLUS
DOCUMENT NUMBER: 136:406855
TITLE: Medicine based on antihyperglycemic microcapsules with prolonged release and method for preparing same
INVENTOR(S): Castan, Catherine; Meyrueix, Remi; Soula, Gerard
PATENT ASSIGNEE(S): Flamel Technologies, Fr.
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002039984	A2	20020523	WO 2001-FR3625	20011119
WO 2002039984	A3	20020711		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

FR 2816840	A1	20020524	FR 2000-14876	20001117
AU 2002020796	A5	20020527	AU 2002-20796	20011119
EP 1333816	A2	20030813	EP 2001-996365	20011119

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: FR 2000-14876 A 20001117
WO 2001-FR3625 W 20011119

AB The invention concerns an oral galenic form for prolonged release of anti-hyperglycemic (metformin) active principles. Said medicine enables to obtain an efficient therapeutic protection over 24 h by overcoming the problems of bypass of the absorption window and the massive localized release of active principles. Therefor, said medicine comprises several thousand anti- hyperglycemic (metformin) microcapsules each consisting of a core comprising at least an anti- hyperglycemic agent and of a coating film applied on the core and enabling the prolonged release in vivo of the

anti- hyperglycemic agent. Said microcapsules have a grain size distribution ranging between 50 and 100 .mu.. The reproducibility of the transit kinetics and hence of bioavailability are very high. There results for the patient a lesser risk of hyperglycemic or hypoglycemic. The invention also concerns the prepn. of said medicine and the use of a plurality of said microcapsules for making an anti- hyperglycemic medicine. The invention is applicable to the treatment of type II diabetes. A soln. of 159.5 g **stearic** acid and 159.5 g Et cellulose in 2870 g isopropanol at 50.degree. was sprayed on 700 g of metformin hydrochloride crystals (av. diam. 100-200 .mu.m). The dissoln. rate of the granules thus obtained was 97.1% after 20 min.

IT **1115-70-4**, Metformin hydrochloride
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medicine based on antihyperglycemic microcapsules with prolonged release and method for prepg. same)

L5 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:51243 CAPLUS
DOCUMENT NUMBER: 136:123633
TITLE: Oral pharmaceutical composition with controlled release and prolonged absorption
INVENTOR(S): Castan, Catherine; Legrand, Valerie; Meyrueix, Remi; Soula, Gerard
PATENT ASSIGNEE(S): Flamel Technologies, Fr.
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002003964	A1	20020117	WO 2001-FR2224	20010710
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2811571	A1	20020118	FR 2000-9047	20000711
FR 2811571	B1	20021011		
EP 1299090	A1	20030409	EP 2001-955397	20010710
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: FR 2000-9047 A 20000711
WO 2001-FR2224 W 20010710

AB The invention concerns a galenic system with prolonged/controlled release of the medicinal and/or nutritional active principle, for oral administration. The aim is to provide a system enabling to obtain with one single tolerable and acceptable dose of active principle, efficient therapeutic protection over 24 h (increasing the bioabsorption time without affecting bioavailability). To achieve this, the invention provides a compn. comprising two controlled release systems assocd. in series, namely: individualized coated particles (microcapsules) of active principle forming an internal phase, the coating comprising a film-forming polymer P1 (Et cellulose), a nitrogenous polymer (polyvinylpyrrolidone), a softener (castor oil) and a lubricant (magnesium stearate), and an external phase of functional carriers: polyelectrolytic hydrophilic polymer: (alginate), neutral hydrophilic polymer (hydroxypropyl Me cellulose) and a gelling additive (calcium acetate), said compn.

spontaneously forming in the presence of water, a cohesive and stable composite macroscopic solid, wherein the external continuous phase is a gelled matrix including the active principle microcapsules. The invention is useful for delayed oral galenic formulation of metformin. A capsule contained metformine hydrochloride 25.47, Ethocel-7 6.60, magnesium stearate 0.89, castor oil 0.72, Plasdone K 29/32 0.72, Kelton HVCR 50.91, Methocel premium K100M 13.12, and calcium acetate 1.57%. Dissoln. rate of the capsule was studied.

IT **1115-70-4**, Metformin hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral pharmaceutical compn. with controlled release and prolonged absorption)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:163422 CAPLUS
DOCUMENT NUMBER: 134:212730
TITLE: Controlled-release lipoic acid
INVENTOR(S): Byrd, Edward A.; Janjikhel, Rajiv
PATENT ASSIGNEE(S): Medical Research Institute, USA
SOURCE: U.S., 14 pp., Cont.-in-part of U.S. Ser. No. 112,623, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6197340	B1	20010306	US 1999-288245	19990408
US 6191162	B1	20010220	US 1999-288253	19990408
CA 2332790	AA	19991202	CA 1999-2332790	19990519
WO 9961004	A1	19991202	WO 1999-US11178	19990519
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9940903	A1	19991213	AU 1999-40903	19990519
EP 1082107	A1	20010314	EP 1999-924394	19990519
R: DE, ES, FR, GB, IT				
JP 2002516270	T2	20020604	JP 2000-550464	19990519
US 2001028896	A1	20011011	US 2001-755890	20010105
US 6572888	B2	20030603		
US 2003039690	A1	20030227	US 2002-226646	20020823

PRIORITY APPLN. INFO.:
US 1998-87203P P 19980528
US 1998-112623 B2 19980709
US 1998-102605P P 19981001
US 1999-288245 A 19990408
WO 1999-US11178 W 19990519
US 2001-755890 A2 20010105

AB A controlled release formulation of lipoic acid is disclosed. The lipoic acid is combined with excipient materials in such a way that those materials protect the lipoic acid from chem. degrdn. in the gastrointestinal tract and provide for gradual release of the lipoic acid. These combined features make it possible to use lipoic acid to reduce serum glucose levels and maintain those levels over time thereby obtaining a range of desired results. A sustained-release tablet contained racemic

.alpha.-lipoic acid coated particles 81, Methocel K100 10, microcryst. cellulose 5, **stearic** acid 3, micronized silica 0.5, and magnesium stearate 0.5%. Efficacy of the formulation in lowering blood glucose level of patients is reported.

IT **1115-70-4**, Metformin hydrochloride.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled-release lipoic acid)

REFERENCE COUNT: 115 THERE ARE 115 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:136991 CAPLUS
DOCUMENT NUMBER: 134:198075
TITLE: Triglyceride-free compositions and methods for enhanced absorption of hydrophilic therapeutic agents
INVENTOR(S): Patel, Mahesh V.; Chen, Feng-Jing
PATENT ASSIGNEE(S): Lipocine, Inc., USA
SOURCE: PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001012155	A1	20010222	WO 2000-US18807	20000710
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6309663	B1	20011030	US 1999-375636	19990817
EP 1210063	A1	20020605	EP 2000-947184	20000710
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003506476	T2	20030218	JP 2001-516502	20000710
US 2001024658	A1	20010927	US 2000-751968	20001229
US 6458383	B2	20021001		

PRIORITY APPLN. INFO.: US 1999-375636 A 19990817
WO 2000-US18807 W 20000710

AB The present invention relates to triglyceride-free pharmaceutical compns., pharmaceutical systems, and methods for enhanced absorption of hydrophilic therapeutic agents. The compns. and systems include an absorption enhancing carrier, where the carrier is formed from a combination of at least two surfactants, at least one of which is hydrophilic. A hydrophilic therapeutic agent can be incorporated into the compn., or can be co-administered with the compn. as part of a pharmaceutical system. The invention also provides methods of treatment with hydrophilic therapeutic agents using these compns. and systems. For example, when a compn. contg. Cremophor RH40 0.30, Arlacel 186 0.20, Na taurocholate 0.18, and propylene glycol 0.32 g, resp., was used, the relative absorption of PEG 4000 as a model macromol. drug was enhanced by 991%.

IT **1115-70-4**, Metformin hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. for enhanced absorption of hydrophilic drugs using combination of surfactants)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:760291 CAPLUS
DOCUMENT NUMBER: 132:83528
TITLE: Development and biopharmaceutical evaluation of controlled release tablets of metformin hydrochloride using a dissolution medium with gradual pH variation
AUTHOR(S): De Pinho, Jose De Jesus R. G.; Storpirtis, Silvia
CORPORATE SOURCE: Laboratorio de Technologia Farmaceutica e de Cosmeticos, Faculdade de Farmacia e Bioquimica, Universidade Federal de Juiz de Fora, Cid. Universitaria, SP, 05389-970, Brazil
SOURCE: Revista Brasileira de Ciencias Farmaceuticas (1999), 35(1), 101-109
CODEN: RBCFFM; ISSN: 1516-9332
PUBLISHER: Universidade de Sao Paulo, Faculdade de Ciencias Farmaceuticas
DOCUMENT TYPE: Journal
LANGUAGE: Portuguese
AB Four formulations of controlled-release tablets contg. 850 mg metformin HCl were prepd. using different amts. of hydroxypropylmethylcellulose and **stearic** acid adjuvants along with std. amts. of other excipients. The prepns. were submitted to dissoln. assays using 6 vessels with paddle app. (1000 mL deaerated distd. water or aq. soln. with gradual pH variation from 1.3 to 7.5; 100 rpm; 37.0.+-.0.5.degree.C; 10 mL aliquots withdrawn at 10, 30, 60, 90, 120, 180, 240, 300, and 360 min). The drug was quantified by UV spectrophotometry at 233 nm. The results showed that the drug release was affected by the tablet adjuvants, but not by pH variations.
IT **1115-70-4**, Metformin hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metformin HCl controlled release tablet development and bioavailability evaluation in media with gradual pH change)
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1977:589462 CAPLUS
DOCUMENT NUMBER: 87:189462
TITLE: Anti-cellulitis composition
INVENTOR(S): Dabis, Georges
PATENT ASSIGNEE(S): Fr.
SOURCE: Fr. Demande, 9 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2320735	A1	19770311	FR 1975-25069	19750812
FR 2320735	B1	19790914		

PRIORITY APPLN. INFO.: FR 1975-25069 19750812
AB Compns. for the transcutaneous treatment of cellulitis comprise at least 1 of the hydrochloride or pamoate salts of metformin, phenformin, butformin, and chlorguanide in combination with an acceptable excipient. For example, a compn. was prepd. contg. TEFOS 1500 10, **stearic** acid 1, liquid petrolatum 8, galactomannan gel 30, metformin-HCl [**1115-70-4**] 5.33, and deionized water 45.67 g. Twice daily administration of the above compn. for 30 days caused a marked and rapid treatment of a previously incurable cellulitis in a female patient.
IT **1115-70-4**
RL: BIOL (Biological study)

(cellulitis treatment with)

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=> file stnguide
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    93.98     107.59

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                   -17.58     -17.58

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AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Aug 22, 2003 (20030822/UP).
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